Patent
Attorney's Docket No. 028722-274

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	
Iatrou, et al.	Group Art Unit: Unassigned
Application No.: Unassigned (Divisional of 09/256,694)	Examiner: Unassigned
Filed: Herewith	
For: SEQUENCES FOR IMPROVING THE EFFICIENCY OF SECRETION OF NON-SECRETED PROTEINS FROM MAMMALIAN AND INSECT CELLS	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This Preliminary Amendment is submitted before the first Office Action on the merits for the above-referenced application. The Examiner is requested to enter this amendment prior to examination on the merits.

In the event that a telephone call could expedite the prosecution of this application, the Examiner is requested to telephone the undersigned at 650-622-2300 (extension 2340).

AMENDMENT

In the Specification:

Please make the following amendments in the specification. Pursuant to 37 C.F.R. §1.121(b)(1)(iii), a marked-up copy of the amended paragraphs in the specification is attached herewith on separate pages.

Please replace the paragraph starting at page 1, line 7, with the following:

--This application is a divisional of U.S. Patent Application Serial No. 09/256,694, filed February 24, 1999, which is a continuation-in-part of U.S. Patent Application Serial No. 09/136,421, filed August 20, 1998 which in turn claims priority to U.S. Provisional Application Serial No. 60/056,871 filed August 21, 1997, all of which are incorporated herein by reference in their entirety.--

Please replace the paragraph starting at page 7, line 4, with the following:

--Figure 4 (SEQ ID NO:13) shows the DNA sequence of the juvenile hormone esterase (JHE) gene from *Heliothis virescens*, Genbank Accession No. J04955 (Hanzlik et al., 1989). The first translation start codon, methionine, is indicated in bold.--

Please replace the paragraph starting at page 7, line 11, with the following:

--Figure 6 (SEQ ID NO:14) shows the DNA sequence of the human granulocyte macrophage colony stimulating factor cDNA. The first translation start codon, methionine, and the translation stop codon are indicated in bold.--

At page 20, after the paragraph ending at line 24, please add the following paragraph:

--This technique would be useful for the extracellular production of non-secretion competent polypeptides from a genetically engineered organism for medical research or veterinary application. For polyclonal or monoclonal antibody generation, this secretion techniques would be coupled with a DNA vaccine vector to induce a humoral immune response against the non-secretion competent polypeptides. For non-secretion competent polypeptides derived from pathogenic organisms, this secretion technique would be coupled with a DNA vaccine vector to induce an immune response for human and animal vaccines.--

Please replace the paragraph starting at page 22, line 22 and continuing on page 23 with the following:

--The DNA module for the secretion of chloramphenicol acetyl transferase (CAT) is shown in Figure 2A. At the 5' end, it contains the complete cDNA coding for the insect secreted protein juvenile hormone esterase (JHE) (Hanzlik et al.) which can be secreted from animal cell hosts. The spacer region (coding for SEQ ID NO:12) contains DNA coding for six histidine residues that are attracted to Ni(II)-NTA chromatography matrices for affinity purification (Kroll 1993). The spacer region also contains a nucleic acid sequence coding for the amino acid sequence DDDDK, which is a cleavage site recognized by the protease porcine intestine enteropeptidase (Kell 1971). The spacer region is bound on each side by a proline residue which encourages the spacer peptide to form its own domain for better access to both the chromatographic purification matrix and the enteropeptidase. The module also contains the DNA sequence coding for CAT.--

Please replace the paragraph starting at page 25, line 9, with the following:

--(i) First 2 oligonucleotides (SEQ ID NOs: 1 and 2) were synthesized (5′ to 3′) coding for region II in Figure 2A:

I. 5'- AAAGGATCCAATGCCACATCATCATCAT
CATCATGGCGGCGGC -3'

II. 5'- AAAACCATGGCCTGGGTCCTTGTCGTCGTC
GTCGCCGCCGCC- 3'--

Please replace the paragraph starting at page 25, line 19, with the following:

-- (ii) Next two mutagenic primers (SEQ ID NOs:3 and 4) (5′ to 3′) were synthesized in order to generate region III in Figure 2A:

I. 5'- GGGCTACCATGGAGAAAAAAATCACTGG -3'

II. 5'- GGGTGCTCTAGAATTTCTGCCATTCATCC -3'--

Please replace the paragraph starting at page 25, line 27 and continuing onto page 26, lines 1-3, with the following:

--(iii) The following two mutagenic primers (SEQ ID NOs: 5 and 6) (5′ to 3′) were synthesized to obtain region I in Figure 2a:

I. 5'- AAAAGGATCCATGACTTCACACGTACTCGC -3'

II. 5'- AAAAGGATCCTTCAAGCGGGCTTCTACTG -3'--

Please replace the paragraph starting at page 28, line 17, with the following:

--(i) First 2 oligonucleotides (SEQ ID NOs: 1 and 7) were synthesized (5′ to 3′) coding for region II in Figure 3A:

I. 5'- AAAGGATCCA ATG CCA CAT CAT CAT CAT CAT CAT GGC GGC GGC -3'

II. 5'- AAAAGC ATG CCC TGG GTC CTT GTC GTC GTC GTC GCC GCC GCC -3'--

Please replace the paragraph starting at page 29, line 1, with the following:

--(ii) The following 2 oligonucleotides (SEQ ID NOs: 8 and 9) were synthesized (5′ to 3′) to obtain region III in Figure 3A:

I. 5'- TGTGGGCATGCAGAGCGTGGCGAAG -3'

II. 5'- CGACATTCAAATCTAGAATAAGTCCCCCTAC -3'--

Please replace the paragraph starting at page 32, line 6, with the following:

--(ii) Next two mutagenic primers (SEQ ID NOs: 10 and 11) (5' to 3') were synthesized:

I. 5'- GAAGGATCCGATGTGGCTGCAGAGCC -3'

II. 5'- CAAGGATCCCTCCTGGACTGGCTCCC-3'--

In the Claims:

Please cancel Claims 1-22, without prejudice or disclaimer.

Please add new Claims 23-36 as follows:

--23. (new) A composition useful to stimulate an immune response, said composition comprising an expression cassette comprising a polynucleotide encoding from its 5' to 3' direction: a) a promoter b) a signal peptide; c) a secretion competent polypeptide; and d) a heterologous protein wherein the polynucleotide sequences encoding (b), (c) and (d) are linked in frame.

24. (new) The composition of claim 23 wherein the secretion competent polypeptide is selected from the group consisting of juvenile hormone esterase and granulocyte macrophage colony stimulating factor.

25. (new) The composition of Claim 23 wherein the polynucleotide further comprises an enhancer.

26. (new) The composition of Claim 23 which is used as a vaccine composition.

27. (new) The composition of Claim 23 wherein the heterologous protein is derived from a pathogenic organism.

28. (new) A method of preventing a pathogenic infection in a mammal, said method comprising administering to the mammal the composition of Claim 27 under conditions wherein, when the cassette is introduced into the cells of the mammal by the administration of the cassette to the mammal, the heterologous protein is expressed and

secreted from the cells, resulting in the production in the mammal of antibodies which prevent infection.

29. (new) A method for generating antibodies to a heterologous protein in a mammal, said method comprising administering to the mammal an expression cassette comprising a polynucleotide encoding from its 5' to 3' direction: a) a promoter; b) a signal peptide; c) a secretion competent polypeptide; and d) the heterologous protein wherein the polynucleotide sequences encoding (b), (c) and (d) are linked in frame under conditions wherein, when the cassette is introduced into the cells of the mammal by the administration of the cassette to the mammal, the heterologous protein is expressed and secreted from the cells, resulting in the production in the mammal of antibodies to the heterologous protein.

30. (new) The method of Claim 29 wherein the secretion competent polypeptide is selected from the group consisting of juvenile hormone esterase and granulocyte macrophage colony stimulating factor.

31. (new) The method of Claim 29 wherein the polynucleotide further comprises an enhancer.

32. (new) The method of Claim 29 wherein said heterologous protein is derived from a pathogenic organism.

33. (new) A method for inducing an immune response in a mammal against a heterologous protein, comprising administering to the mammal an expression cassette comprising a polynucleotide encoding from its 5' to 3' direction: a) a promoter; b) a signal peptide; c) a secretion competent polypeptide; and d) the heterologous protein wherein the polynucleotide sequences encoding (b), (c) and (d) are linked in frame.

34. (new) The method of Claim 33 wherein the secretion competent polypeptide is selected from the group consisting of juvenile hormone esterase and granulocyte macrophage colony stimulating factor.

35. (new) The method of Claim 33 wherein the polynucleotide further comprises an enhancer.

36. (new) The method of Claim 33 wherein said heterologous protein is derived from a pathogenic organism.--

REMARKS

Specification Amendments:

The specification has been amended on page 1 to update the related applications information.

The specification has also been amended on page 20 to clarify the scope of the present invention. The language added can be found on page 16, line 25 to page 17, line 1 of U.S. Patent Application Serial No. 09/136,421, filed August 20, 1998, which is the grandparent application of this application and has been incorporated herein by reference in its entirety. (Applicants note that U.S. Patent Application Serial No. 09/136,421 has now issued as U.S. Patent No. 6,037,150; the added paragraph is also found at column 8, lines 55-65 of this patent).

The specification has been further amended to insert references to the SEQ ID numbers in the enclosed sequence listing.

No new matter has been added by this amendment. The Examiner is hereby requested to enter this amendment.

Claim Amendments:

Claims 1-22 have been canceled, without prejudice or disclaimer. Applicants specifically reserve the right to file appropriate continuing and/or divisional application(s) drawn to the subject matter of these claims.

New Claims 23-36 have been added, which are drawn to compositions useful to stimulate an immune response, methods of generating antibodies, and methods of inducing

an immune response. Support for these claims may be found, for example, at the Abstract; page 10, lines 5-19; page 14, lines 3-12; and page 20, the paragraph added after line 24.

No new matter has been added by these amendments. The Examiner is hereby requested to enter these amendments.

Sequence Listing:

Applicants submit herewith a paper copy of the Sequence Listing and request that this sequence listing be entered into the specification.

Applicants also request transfer of the computer readable form (CRF) from the parent application, U.S. Application Serial No. 09/256,694, filed February 24, 1999. In accordance with 37 C.F.R. §1.821(e), please use the only CRF filed in that application as the computer readable form for the instant application. It is understood that the USPTO will make the necessary change in application number and filing date for the instant application.

Pursuant to 37 C.F.R. §1.821(f), the undersigned hereby states that the information recorded in the aforementioned CRF is identical to the written Sequence Listing contained in the paper copy submitted herewith, and that the submission does not include any new matter.

Conclusions:

Applicants request that the above amendments be entered prior to examination on the merits of this application. Early and favorable examination is hereby requested.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
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Date: February 26, 2002

Attachment to Preliminary Amendment dated February 26, 2002
Marked-up Copy of Amendments in the Specification

On page 1, please amend the paragraph starting on line 7 as follows:

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On page 29, please amend the paragraph starting on line 1 as follows:

(ii) The following 2 oligonucleotides (SEQ ID NOs: 8 and 9) were synthesized (5′ to 3′) to obtain region III in Figure 3A:

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II. 5'- CGACATTCAAATCTAGAATAAGTCCCCCTAC -3'

On page 32, please amend the paragraph starting on line 6 as follows:

(ii) Next two mutagenic primers (SEQ ID NOs: 10 and 11) (5' to 3') were synthesized:

III. 5'- GAAGGATCCGATGTGGCTGCAGAGCC -3'

IV. 5'- CAAGGATCCCTCCTGGACTGGCTCCC-3'